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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

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Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6002

November 13, 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED
Richard M. Klein
President/CEO
Sybron Chemicals Inc.
Birmingham Road
Birmingham, New Jersey 08011

FILE NO.:01-NWJ-03

Dear Mr. Klein:

This letter concerns an inspection of your facility located at Birmingham Road, Birmingham, New Jersey conducted by the U.S. Food and Drug Administration on March 1 through March 10, 2000. During the inspection our investigators documented significant deviations from current Good Manufacturing Practices (cGMPs) in the manufacture of Active Pharmaceutical Ingredients (APIs).

The deviations cause your API product (Sodium Polystyrene Sulfate, USP) to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). Section 501(a)(2)(B) requires that drugs be manufactured, processed, packed, and held in accordance with cGMPs. No distinction is made between active pharmaceutical ingredients and finished pharmaceutical ingredients. Failure to comply with cGMPs constitutes a failure to comply with the requirements of the Act.

The significant observations are as follows:

1. Your firm failed to adequately clean and maintain the process equipment at appropriate intervals to prevent contamination or malfunction of the equipment. For example, the neutralization tank lid was heavily encrusted with inches of unknown debris. The lid was bowed creating gaps between the reaction vessel and the lid. The plastic, wood, hinges, and bolts were corroded and there was a hole in the center of the inspection cover.

2. Failure to establish standard operating procedures (SOPs) or document the performance qualifications and maintenance of the analytical equipment used in the testing and the release of the product Sodium Polystyrene Sulfonate, USP.

3. No raw data for the USP Test, Sodium Polystyrene Sulfonate, USP:

   - Water, Method 921, Karl Fisher H2O: no calibration data

   - Limit of Ammonium Salts: no indications of weight

   - Sodium Content: no standard curve; no indication of how the standard curve was prepared; no indication what instrument was used; no indication of sample weight and what balance used.

   - Potassium Exchange Capacity: no standard curve; no indication of how the standard curve was prepared; no indication what instrument was used; no indication of sample weight and what balance used.

   Additionally, your firm has no SOP for maintaining data. The firm does not maintain chromatograms, system suitability records or instrument calibration data.

4. Your batch production and control records are inadequate in that they do not include labeling, sampling instructions, and signed certificates of analysis for finished product release.

5. Your formalized training program is inadequate in that it does not address current good manufacturing practices. There is no documentation that your QA/QC Laboratory personnel received any cGMP training.

We received your written response dated April 19, 2000 concerning the above observations. Our review of this response shows that you have not adequately addressed the following issues:

- You addressed lid replacement efforts, but did not address the observation of failure to clean and maintain process equipment. Your response to the lack of batch production records is inadequate since you responded that in the future you can provide archived records as requested, but made no

promises to keep records in such a way that they will be readily available for review. You did not address the observation of lack of documentation. You explained repair work to the neutralizer lid in terms of normal repairs and maintenance, but did not address the lack of documentation for repairs to the lid.

- You promise to establish logbooks and use a contract service to perform qualifications. You do not address maintenance or calibration records.

- You do not appear to understand the importance of recording exact weights used when preparing solutions for analysis.

- We accept your explanation of the power outage event, yet the observation demonstrates your failure to establish and maintain proper records. We consider this a systemic problem.

- We continue to be concerned that you do not appear to understand the necessity of maintaining a record of batch release by a responsible individual within your quality control unit.

- We are concerned that you do not appear to understand the significance of training your employees in CGMP's. Your response to the observation is explained in terms of material safety considerations.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with the requirements of the Act. Failure to comply with cGMP constitutes a failure to comply with the requirements of the Act. We request that you take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. This includes seizure and/or injunction.

Federal agencies are advised of the issuance of all Warning Letters regarding drugs and devices so that they may take this information into account when considering the award of contracts. Additionally, new drug applications (NDAs), abbreviated new drug applications (ANDAs) or export approval requests may not be approved until the aforementioned cGMP violations are corrected.

You should notify this office in writing within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to the Food and Drug Administration, New Jersey District Office, 10 Waterview Blvd, 3rd Floor, Parsippany, New Jersey 07054, Attention: Andrew Ciaccia, Compliance Officer.

Very truly yours,

Douglas I. Ellsworth
District Director
New Jersey District Office

AC:slm

Cc: [redacted]